Attorney Docket No. 5253.200-US PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

#8 6/16/99 T. Gray

In re Application of: Blinkovsky *et al.*

Serial No.: 09/080,127 Group Art Unit: 1645

Filed: May 15, 1998 Examiner: Weatherspoon, J.

For: Polypeptides Having Aminopeptidase Activity And Nucleic Acids Encoding Same

DECLARATION UNDER 37 CFR §1.132

Hon. Assistant Commissioner for Patents
Washington, DC 20231

Sir:

I, Alexander Blinkovsky, declare that:

1. I received a Ph.D. from the Moscow State University in Moscow, Russia in 1984, in the area of chemical enzymology. I have worked in the field of protein chemistry for 21 years. I am currently employed by Novo Nordisk Biotech, Inc., Davis, California as a Senior Scientist, where I have been employed since 1994.

2. I am a co-inventor of patent application serial no. 09/080,127 and am familiar with the prosecution history thereof including the Office Action dated December 8, 1998.

3. I respectfully disagree with the Office Action statements: "Kauppinen *et al.* disclose an isolated polypeptide having aminopeptidase activity wherein said polypeptide is encoded by a nucleic acid sequence which hybridizes with the nucleic acid sequence or a subsequence of SEQ ID NO. 1 or its complementary strand (as stated in instant claim 1) (see entire reference) and wherein said polypeptide is obtained from an *Aspergillus oryzae* strain (see entire reference, for example pages 4 and 6). Kauppinen *et al.* also disclose a polypeptide comprising a fragment of the sequence of instant SEQ ID NO. 2, a method for producing said polypeptide comprising recovering said polypeptide from said *Aspergillus* strain (see entire reference) and compositions comprising said aminopeptidase as recited in the instant claims 44-45 (see entire reference)."

4. In my opinion, the *Aspergillus oryzae* aminopeptidase disclosed by Kauppinen *et al.* (hereinafter the "Kauppinen aminopeptidase") is distinguishable from the aminopeptidases claimed in the subject invention.

5. A comparison of the percent identity was made between the amino acid sequence of the Kauppinen aminopeptidase and the aminopeptidase of SEQ ID NO. 2. The degree of identity was determined by the Clustal method (Higgins, 1989, *CABIOS* 5: 151-153) using the LASERGENE™ MEGALIGN™ software (DNASTAR, Inc., Madison, WI) with an identity table and the following multiple alignment parameters: Gap penalty of 10 and gap length penalty of 10. Pairwise alignment parameters were Ktuple=1, gap penalty=3, windows=5, and diagonals=5.

The comparison showed that the amino acid sequence of the Kauppinen aminopeptidase is 13.5% identical to the aminopeptidase of SEQ ID NO. 2. This low degree of identity between the two aminopeptidases indicates that the corresponding genes, and subsequences of the genes which encode polypeptide fragments having aminopeptidase activity, would not hybridize under medium stringency conditions as defined by prehybridization and hybridization at 42°C in 5X SSPE, 0.3% SDS, 200 μg/ml sheared and denatured salmon sperm DNA, and 35% formamide for medium and wash conditions of three times each for 15 minutes using 2 x SSC, 0.2% SDS at 55°C, following standard Southern blotting procedures.

6. All statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true and further that I make these statements with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated: June 3, 1999

By: Alexander Blinkovsky
Alexander Blinkovsky